

WHAT IS CLAIMED IS:

1. A composition for affecting weight loss comprising a first compound and a second compound, wherein said first compound is an opioid antagonist and said second compound causes increased agonism of a melanocortin 3 receptor (MC3-R) or a melanocortin 4 receptor (MC4-R) compared to normal physiological conditions.

2. The composition of claim 1, wherein said opioid antagonist antagonizes an opioid receptor selected from a  $\mu$ -opioid receptor (MOP-R), a  $\kappa$ -opioid receptor, and a  $\delta$ -opioid receptor.

3. The composition of claim 1, wherein said opioid antagonist is selected from the group consisting of alvimopan, norbinaltorphimine, nalmefene, naloxone, naltrexone, methylnaltrexone, and nalorphine, and pharmaceutically acceptable salts or prodrugs thereof.

4. The composition of claim 1, wherein said second compound triggers the release of  $\alpha$ -melanocyte stimulating hormone ( $\alpha$ -MSH).

5. The composition of claim 4, wherein said second compound increases the extracellular serotonin concentrations in the hypothalamus.

6. The composition of claim 5, wherein said second compound is selected from the group consisting of a selective serotonin reuptake inhibitor (SSRI), a serotonin 2C agonist, and a serotonin 1B agonist.

7. The composition of claim 6, wherein said second compound is selected from the group consisting of fluoxetine, fluvoxamine, sertraline, paroxetine, citalopram, escitalopram, sibutramine, duloxetine, and venlafaxine, and pharmaceutically acceptable salts or prodrugs thereof.

8. The composition of claim 1, wherein said first compound is naltrexone and said second compound is fluoxetine.

9. The composition of claim 1, wherein said first compound is naltrexone and said second compound is bupropion.

10. A method of affecting weight loss, comprising identifying an individual in need thereof and treating that individual to antagonize opioid receptor activity and to enhance  $\alpha$ -MSH activity.

11. The method of claim 10, wherein said individual has a body mass index greater than 25.
12. The method of claim 10, wherein opioid receptor activity is antagonized by administering an opioid receptor antagonist.
13. The method of claim 12, wherein the opioid receptor antagonist is a MOP receptor antagonist.
14. The method of claim 10, wherein the opioid receptor antagonist is selected from alvimopan, norbinaltorphimine, nalmefene, naloxone, naltrexone, methylnaltrexone, and nalorphine, and pharmaceutically acceptable salts or prodrugs thereof.
15. The method of claim 10, wherein  $\alpha$ -MSH activity is enhanced by administering a compound that triggers the release of  $\alpha$ -MSH or increases the activity of neurons that express  $\alpha$ -MSH.
16. The method of claim 15, wherein said compound is a selective serotonin reuptake inhibitor (SSRI) or a specific 5-HT receptor agonist.
17. The method of claim 16, wherein said SSRI is selected from fluoxetine, fluvoxamine, sertraline, paroxetine, citalopram, escitalopram, sibutramine, duloxetine, and venlafaxine, and pharmaceutically acceptable salts or prodrugs thereof.
18. The method of claim 10, wherein said treating step comprises administering to said individual a first compound and a second compound, wherein said first compound is an opioid antagonist and said second compound enhances  $\alpha$ -MSH activity.
19. The method of claim 18, wherein said first compound and said second compound are administered nearly simultaneously.
20. The method of claim 10, wherein said treating step comprises administering to said individual a first compound and a second compound, wherein said first compound is an opioid antagonist and said second compound enhances  $\alpha$ -MSH activity.
21. The method of claim 10, wherein said individual does not suffer from depression, Prader-Willi syndrome, or binge eating disorder.